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Asbestos Exposure, Smoking Habits, and Cancer Incidence Among Production and Maintenance Workers in an Electrochemical Plant

18

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The incidence of cancer was studied in a cohort of 287 men who were exposed to asbestos at a nitric acid production plant from 1928 onwards. During the observation period from 1953 through 1980 all cancer cases among the cohort members were identified in The Cancer Registry. For the whole cohort 42 cases of cancer were observed versus 30.6 expected. The figures for cancer of the lungs and pleura combined were 17 observed versus 3.7 expected. The corresponding figures for a heavily exposed subcohort were 11 observed and 1.2 expected. In that group there was also an increased incidence of colon cancer with 3 cases observed against 0.8 cases expected. Within the whole cohort four cases of pleural and one case of peritoneal malignant mesothelioma were found. There was also an increased incidence of malignant melanoma of the skin with 3 cases observed against 0.6 expected. For cancer cases that were registered as of unknown origin there were 7 cases observed and 1.4 expected. There was no increased rate ratio for cancer at any site before 20 years after the first asbestos exposure. The smoking habits of all cohort members were recorded and the relative rates for lung cancer were calculated in relation to smoking habits. In common with previous studies the results indicate a multiplicative model for the interaction between asbestos exposure and smoking in regard to lung cancer risk.

Key words: electrochemical industry, asbestos exposure, cancer incidence, smoking habits

INTRODUCTION

During the last decades the cancer hazard due to asbestos dust exposure has been extensively investigated. Epidemiologic studies have been carried out among exposed workers in typical asbestos trades such as asbestos mining [McDonald et al, 1980; Wagner et al, 1960], asbestos textile production [Doll, 1955; Newhouse et al, 1972], insulation [Selikoff et al, 1979], shipbuilding [Elmes and Simpson, 1977; Stumphius, 1971], and asbestos cement production [Ohlson and Hogstedt, 1982; Finkelstein, 1983]. Studies on asbestos-exposed workers from other trades include

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the studies of mesothelioma among asbestos-exposed US machinists [Mancuso, 1983] and of mesothelioma and mortality after crocidolite exposure during gas mask manufacture [McDonald and McDonald, 1978; Wignall and Fox, 1982]. Lilis et al [1979] studied the prevalence of asbestosis in maintenance workers at a chemical industry. They found that 24% of the workers had parenchymal fibrosis and 14% had pleural fibrosis. These results indicate that asbestos has also been extensively used for maintenance purposes within chemical industries. In 1971 a report was presented on 26 mesothelioma patients, of whom 24 had been employed within two large chemical plants [Bittersohl and Ose, 1971]. To our knowledge there have been no other studies on cancer hazard in asbestos-exposed workers in chemical industries.

In a nitric acid production plant within an electrochemical industrial complex located in southern Norway, asbestos has been extensively used since 1928 as a jointing material in granite towers where nitric acid was synthesized (Fig. 1), and as a gasket material in various processes. During the construction of this plant in 1928 and 1929 a group of young men was heavily exposed to asbestos dust. The occurrence of cancer in that group has been reported in a previous paper [Hilt et al, 1981]. The purpose of the present study was to investigate the incidence of cancer in relation to asbestos exposure and smoking habits in a cohort consisting of all production and maintenance workers at the same plant.

PERSONS AND METHODS

Study Population

The study cohort consists of all men who had been regularly exposed to asbestos at the nitric acid production plant between 1928 and 1980. Those who were first

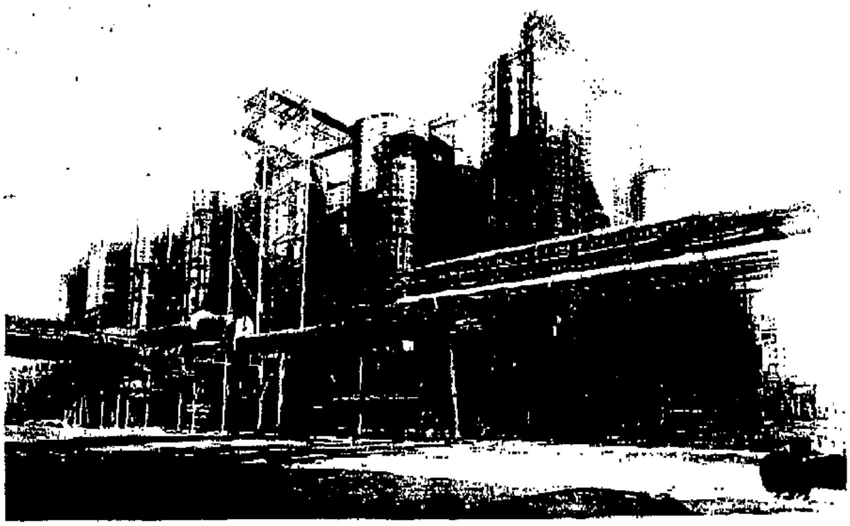

Fig. 1. The 30-m-high nitric acid towers built of granite blocks. The grooves between the blocks were plugged with asbestos and waterglass.

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exposed at the plant after 1961 were excluded because of too short an observation period. As registration of cancer cases in the Norwegian Cancer Registry is reckoned to be comprehensive from January 1, 1953, the study cohort was also restricted to those who were alive at that date. Eleven men in the cohort who had died before that time were excluded. Information on the subjects who were to be included in the cohort was mainly provided by the personnel department of the plant, and in some cases additional information was also collected from fellow workers. At the time the cohort was identified, no information about the health outcome of the workers was known, and only exposure criteria were used for selection of the cohort members. Information on the smoking habits of deceased cohort members was obtained from the health department at the plant, from medical records at local hospitals, and in some cases from their relatives.

Methods

In 1951, legislation was introduced requiring that all histologically verified new cases of cancer in Norway be reported to the nationwide Norwegian Cancer Registry. The registration is based on compulsory reports to the Cancer Registry from all Norwegian hospitals and pathological laboratories. All death certificates where cancer is mentioned are reported to the Cancer Registry from the Central Bureau of Statistics. Age- and sex-specific incidence rates have been published by the Cancer Registry for all cancer sites for each year from 1953 through 1976 (Cancer Registry of Norway, 1972, 1973, 1978). By use of a method described by Pedersen et al [1973], the incidence rates for the whole country for 5-year age groups were used to calculate the expected incidence of cancer at different locations during the observation period from 1953 through 1980.

The unique personal number assigned to every person in Norway was used to link the cohort with all cancer cases registered in the Cancer Registry. In this way it was possible to identify every cancer case that had occurred among the cohort members during the observation period.

The Cancer Registry has presented figures on the geographical variations in cancer incidence in Norway. These figures show that the rates of lung cancer in the county of Telemark, where the present study was carried out, were between 0.80 and 0.95 of the national figures during the follow-up period. Therefore, it is unlikely that geographical variations in cancer incidence would lead to an underestimation of the expected figures in the present study.

As it was known that cases of malignant mesothelioma located both in pleura and peritoneum had been frequently overlooked in previous years, all available histological preparations from gastrointestinal and thoracic tumors that had occurred among the cohort members were reviewed.

The calculations of a 95% confidence interval for the observed versus expected number of cancer cases were based on the assumption that the observed number of cases followed a Poisson distribution.

Asbestos Exposure

Information on asbestos exposure in each type of job in the nitric acid production was used to divide the study group into a heavy- and a light-exposure subcohort. The asbestos dust exposure was presumably very heavy for the workers who were employed in the "fiber hut," where asbestos was mixed with waterglass in order to

make jointing material for the granite towers. Also the men who placed the jointing material in the grooves in these towers had quite a dusty job. These two groups of workers are here reckoned to belong to the heavily exposed group. The group referred to as lightly exposed consists of all lightly and moderately exposed maintenance workers such as mechanics, plumbers, and welders, and the production workers whose exposure to asbestos dust has mostly been indirect. Twelve workers had been employed at workplaces at the plant with both heavy and light exposure. In this study they were placed in exposure subcohorts according to the longest duration of specific asbestos exposure at the different workplaces.

The exact work experience of the deceased cohort members prior to their employment at the nitric acid plant was not known. A detailed occupational history was taken for all living cohort members, and there is no reason to assume that there had been a selection of previously asbestos-exposed workers for work at the nitric acid plant. There were only a few workers who had knowledge of any asbestos exposure, e.g., as sailors or shipyard workers, prior to employment at the plant. Only one of the still-living cohort members had been heavily exposed to asbestos as an insulator at a shipyard before he started at the plant.

According to information supplied by the firm that delivered asbestos to the plant and by former employees, crocidolite asbestos was mostly used in the earliest years, whereas from the 1940s onwards both amphiboles and serpentines were employed.

In addition to the exposure to asbestos dust the workers at the plant were also exposed to chemical agents such as nitrous gases, nitric acid vapors, and ammonia.

Because of difficulties with the identification of all workers from the lightly exposed group with short exposure, only workers with at least 1 year of exposure at the plant were included in the lightly exposed subcohort. No such lower limit of exposure time was applied for the heavily exposed group.

Interaction With Smoking

As smoking per se is an important factor in the development of lung cancer, it is of interest to observe the smoking habits of subjects in epidemiologic studies of lung cancer caused by other factors than smoking. Because of the suggested multiplicative mode of interaction between smoking and asbestos in the promotion of lung cancer [Berry et al, 1972; Hammond et al, 1979; Saracci, 1977; Selikoff et al, 1968; Selikoff et al, 1980a], this is particularly the case in studies of lung cancer caused by asbestos exposure. In the present study different sources were used to record the smoking habits of all cohort members.

As part of the migrant study [Reid, 1966], the smoking habits of a countrywide sample of 11,979 Norwegian men born between 1895 and 1929 were surveyed in 1965. In order to study the relative rates of cancer at different sites in relation to smoking habits, this group was followed separately from 1966 through 1977 [Lund and Zeiner-Henriksen, 1981]. In the present study there were 215 men who were born between 1895 and 1929 and who were still alive on January 1, 1966. Their lung cancer rates during the period from 1966 through 1977, for the different smoking categories based on their smoking habits in 1965, were adjusted for age and compared with the lung cancer rates from the follow-up of the migrant study. Both past and current smokers were reckoned as smokers in the migrant study population as well as in the present study population.

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Another way to study the effect of smoking as a confounder is the quantitative elucidation of the confounding by use of the method described by Axelson [1978]. When the distribution of a confounder within the study and reference populations and the effect of the confounder in terms of relative rates for a particular disease are known, it is possible to calculate the amount of confounding as a result of a different distribution of the confounder within the two populations. In the present study the relative lung cancer rates for different smoking habits in the male population [Lund and Zeiner-Henriksen, 1981] were applied for the reference population. In the calculations for the study population relative lung cancer rates for asbestos-exposed smokers, ex-smokers, and never-smokers [Hammond et al, 1979] were applied.

RESULTS

The study cohort consists of 287 men, with 190 and 97 in the lightly and the heavily exposed groups, respectively. By January 1, 1981, 149 of the cohort members were still alive and 138 had died. Figure 2 shows the recruitment to, and the number of men in, the study population for each decade from 1928 on. Table I shows the mean age of the workers at their first asbestos exposure, the mean duration of their exposure at the plant, the mean duration from first exposure to the end of observation for each cohort member, and the number of person-years under observation for the lightly and heavily exposed, subcohorts. The two groups are rather similar in all parameters except for the mean duration of exposure, which is 7 years in the heavily exposed group and 15 years in the lightly exposed group.

Table II presents the observed and expected number of deaths among the cohort members in the observation period from 1953 through 1980. An increased mortality can be observed both in the heavily and the lightly exposed subcohorts.

Table III presents the observed and expected number of all cancers and selected cancer forms for the cohort during the observation period. In addition to the cancer

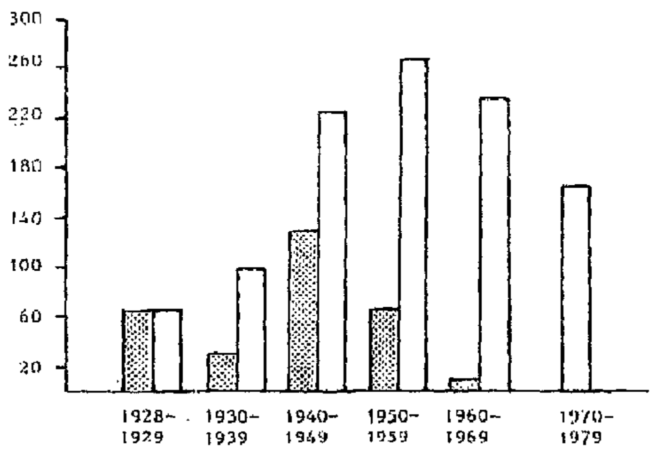

Fig. 2. Number of workers entering the cohort for each decade from 1928 through 1961 ▨. Total number of men under observation in the cohort □.

TABLE I. Age at First Exposure, Exposure Time, Time From First Exposure, and Number of Person-Years at Observation for the Heavily and Lightly Exposed Subcohorts

Exposure subcohort	Mean age at first exposure	Mean duration of exposure (years)	Mean time from first exposure (years)	Person-years under observation
Lightly exposed group (n = 190)	33 (17–59)	15 (1–45)	32 (10–52)	4,410.5
Heavily exposed group (n = 97)	31 (15–53)	7 (0.3–48)	36 (10–52)	1,980.5
All (n = 287)	32.7	12.3	32.9	6,391

Values in parentheses are ranges.

TABLE II. Observed (O) and Expected (E) Number of Deaths From All Causes Observed in the Cohort During the Observation Period, 1953–1980

Exposure subcohort	O	E	O/E
Lightly exposed group (n = 190)	75	69.9	1.07
Heavily exposed group (n = 97)	63	46.9	1.34
All (n = 287)	138	116.7	1.18

locations that are mentioned specifically in Table III, there were among the cohort members three cases of cancer of the prostate, and one case each of leukemia, urine bladder cancer, larynx cancer, and cancer of the mouth. Among the cohort members there were five histologically verified cases of malignant mesothelioma. One of these cases was already registered in the Cancer Registry as a cancer with pleural localization (ICD 162.2, 7th revision). In addition there were three cases of histologically verified pleural malignant mesothelioma that had been registered as lung cancer (ICD 162) in the Cancer Registry. Among the tumors that were histologically revised in connection with the study, there was one abdominal cancer that had been registered as cancer of the stomach (ICD 151), to which revision had assigned malignant mesothelioma of peritoneum as the most probable diagnosis. In Table III these cases are referred to as cancer of lung and pleura and as cancer of the stomach.

As shown in Table III, both the lightly and the heavily exposed subcohort show an increased incidence of cancer of lung and pleura. For the lightly exposed group the observed-to-expected ratio (O/E ratio) was 2.4 with a 95% confidence interval (ci) of 0.92–5.44 (two-tailed p value = 0.084), which could be regarded as of borderline statistical significance. For the heavily exposed group the ratio was 8.9 with 95% ci of 4.6–16.4 ($p = 0.00002$). For colon cancer there is an increased incidence among the heavily exposed group, but with an O/E ratio of 3.9 and a 95% ci of 0.77–10.96 ($p = 0.095$) this result is not statistically significant. The incidence of malignant melanoma of the skin shows a statistically significant increase for the whole cohort with an O/E ratio of 5.1 and a 95% ci of 1.03–14.61 ($p = 0.046$). For cancer of unknown origin there is also an increase in the incidence both for the lighdy exposed subcohort ($p = 0.005$) and for the whole cohort ($p = 0.001$).

TABLE III. Observed (O) and Expected (E) Number of Selected Cancer Forms in the Cohort During the Observation Period, 1953–1980*

Types of cancer	Lightly exposed group				Heavily exposed group				Total cohort			
	O	E	O/E	95% ci	O	E	O/E	95% ci	O	E	O/E	95% ci
All cancers	19	19.9	0.95	0.6–1.5	23	10.7	2.2	1.4–3.2	42	30.6	1.4	1.0–1.9
Lung and pleura (ICD 162–163)[a]	6(1)	2.5	2.4	0.9–5.4	11 (3)	1.2	8.9	4.6–16.4	17	3.8	4.5	2.6–7.2
Stomach (ICD 151)	0	2.7			3 (1)	1.6	1.9	0.4–5.5	3	4.3	0.7	0.1–2.0
Colon (ICD 153)	2	1.4	1.4	0.2–5.2	3	0.8	3.9	0.8–11.0	5	2.2	2.3	0.7–5.3
Malignant melanoma of the skin (ICD 190)	2	0.4	4.8	0.6–18.1	1	0.2			3	0.6	5.1	1.0–14.6
Cancer of unknown origin (ICD 199)	5	0.9	5.4	1.8–13.0	2	0.5	4.0	0.5–14.5	7	1.4	5.5	2.0–10.3

*Values in parentheses are the numbers of malignant mesothelioma.

[a]International Classification of Diseases 7th revision.

The lightly exposed subcohort was subdivided into production workers and maintenance workers in order to study the incidence of cancer in each of these two groups. Among the production workers there was a total of 8 cases of cancer and 14.8 expected. With regard to lung cancer there were 3 cases observed and 1.9 expected, and for cancer of unknown origin there was 1 case observed and 0.7 expected. The maintenance workers from the lightly exposed subcohort had a statistically significant increase in the incidence of all cancers with 11 cases observed and 5.1 cases expected (O/E ratio 2.2, 95% ci 1.1–3.9). For cancer of lung and pleura there were 3 cases observed and 0.6 cases expected (O/E ratio 5.0, 95% ci 1.03–14.61), and for cancer of unknown origin there were 4 cases observed and 0.2 expected (O/E ratio 21.0, 95% ci 5.5–51.2).

As shown in Table IV, the mean duration of exposure for the lung cancer cases in the study cohort was 15.8 years and 9.6 years for the heavily and lightly exposed subcohorts, respectively. For the mean experienced latent period for lung cancer, here defined as the duration from first asbestos exposure to the time of diagnosis, Table IV shows no difference between the two groups.

Table V presents the age-adjusted lung cancer rates per 1,000 during a follow-up from 1966 through 1977 for the 215 cohort members born between 1895 and 1919 and who were alive on January 1, 1966. Their lung cancer rates are shown in relation to smoking habits and are compared with the results from the follow-up from 1966 through 1977 of a general population sample from the migrant study [Lund and Zeiner-Henriksen, 1981]. The age-adjusted lung cancer rates per 1,000 for the 182 cohort members who were smokers was 47.8. As there were only 33 cohort members who had never smoked before 1965, no lung cancer cases were expected among these cohort members during the follow-up period. From Table V it can be calculated that the ratio between asbestos-exposed smokers and smokers unexposed to asbestos was

TABLE IV. Mean Duration of Asbestos Exposure, and Mean Latent Period for the Lung Cancer Cases That Occurred in the Study Cohort

	Duration of exposure	Experienced latent period
Lightly exposed group (n = 6)	15.8 (1–37)	34 (30–40)
Heavily exposed group (n = 11)	9.6 (1–27)	37.5 (27–51)
All (n = 17)	11.8	36.3

TABLE V. Age-Adjusted Lung Cancer Rates per 1,000 in Relation to Smoking Habits in the Present Study Population and in a General Population Sample During a Follow-up, 1966–1977

	General population sample (not asbestos-exposed) (n = 11,979)	Study population (asbestos-exposed) (n = 214)
Nonsmokers	1.9 (7)[a]	— (0)
Smokers	11.1 (111)	47.8 (9)

[a]Values in parenthesis are numbers of cases.

4.3. The ratio between asbestos-exposed smokers and never-smokers unexposed to asbestos was 25.2

In 1965 the smoking habits of a countrywide population sample were 55.6% smokers, 21.8% ex-smokers, and 22.6% never-smokers [Lung and Zeiner-Henriksen, 1981]. In the present study population there was a higher rate of smokers, with 71.7% smokers, 11.9% ex-smokers, and 16.4% never-smokers. The amount of confounding caused by these different smoking habits was estimated by use of the method described by Axelson [1978]. When the calculations also account for the known synergistic interaction between asbestos and smoking, the increase in lung cancer rates in the study population, as a result of higher compared to lower rates of smoking, was 1.87.

The mean latent period for the 17 lung cancer cases among the cohort members was 36.3 (27–51) years. Table VI presents the ratios for cancer of lung and pleura, cancer of unknown origin, and colon cancer in relation to the time passed since first asbestos exposure of the cohort members. There is no increased incidence of any cancer until 20 years after the first exposure, and a statistically significant increase in the O/E ratio for cancer of lung and pleura and cancer of unknown origin first appears between 30 and 39 years subsequent to the first asbestos exposure. For cancer of lung and pleura there is also a significantly increased incidence more than 40 years after the first exposure. The five cases of colon cancer occurred 15, 27, 30, 31, and 35 years after these patients' first exposure to asbestos.

The cause of death is known for 10 of the 11 men who died before 1953 and who were excluded from the study cohort. Two of them died from cancer of the stomach, one from cancer of the pancreas, one from malignant mesothelioma of the pleura, and two men were given the diagnosis "cancer abdominis." The mean latent period from first asbestos exposure for these cancer cases was 19.8 (13–24) years. Even though no rate ratios could be calculated on the basis of these cancer cases, there is a possibility that some of these cancers were associated with the previous asbestos exposure.

DISCUSSION

In common with other cancer incidence and mortality studies within various groups of asbestos-exposed workers, the present study from an electrochemical plant shows an increased incidence of cancer in workers previously exposed to asbestos. The incidence of lung cancer and cancer of unknown origin was increased both in the heavily exposed subcohort and among the maintenance workers who were reckoned to belong to the lightly exposed subcohort. The observed increase in the incidence of cancer at all sites among these workers can be explained by the raised incidence of these two cancer forms. Among the lightly exposed production workers there was an increase in the incidence of lung cancer with an O/E ratio of 1.6, but this was not statistically significant. As for cancer of the colon there was a statistically insignificant raised incidence among the heavily exposed workers, with 3 cases observed and 0.8 expected.

The increased O/E ratio for death from all causes both in the heavily and the lightly exposed subcohorts (Table II) can probably be explained by the increase in the incidence of certain cancer forms. If the excess number of lung cancer cases among

TABLE VI. Observed (O) and Expected (E) Number of Selected Cancer Forms in the Cohort During the Observation Period 1953–1980 in Relation to Time Passed Since First Exposure to Asbestos

Years since first exposure	Cancer of the lung and pleura (ICD 162–163)				Colon cancer (ICD 153)				Cancer of unknown origin (ICD 199)				All other forms of cancer			
	O	E	O/E	95% ci	O	E	O/E	95% ci	O	E	O/E	95% ci	O	E	O/E	95% ci
1–19	0	0.7			1	0.4			0	0.2			1	4.8		
20–29	2	1.2	1.7	0.2–6.0	1	0.8			2	0.5	4.0	0.5–14.5	5	8.2	0.6	0.2–1.4
30–39	11	1.2	9.2	4.6–16.4	3	0.7	4.3	0.9–12.5	4	0.5	8.0	2.2–20.5	5	6.9	0.7	0.2–1.7
40+	4	0.7	5.7	1.6–14.6	0	0.3			1	0.2			2	3.3	0.6	0.1–2.2

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